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(54) Title: ANTI-AMYLOID BETA ANTIBODIES AND THEIR USE

(57) Abstract: The present invention relates to antibody molecules capable of specifically recognizing two regions of the R-A4 peptide, wherein the first region comprises the amino acid sequence AEFRHDSGY as shown in SEQ ID NO: 1 or a fragment thereof and wherein the second region comprises the amino acid sequence VHHQKLVFFAEDVG as shown in SEQ ID NO: 2 or a fragment thereof. Furthermore, nucleic acid molecules encoding the inventive antibody molecules and vectors and hosts comprising said nucleic acid molecules are disclosed. In addition, the present invention provides for compositions, preferably pharmaceutical or diagnostic compositions, comprising the compounds of the invention as well as for specific uses of the antibody molecules, nucleic acid molecules, vectors or hosts of the invention.

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# INTERNATIONAL SEARCH REPORT

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#### A. CLASSIFICATION OF SUBJECT MATTER

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According to International Patent Classification (IPC) or to both national classification and IPC

### B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, SEQUENCE SEARCH, CHEM ABS Data

### C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 39796 A (HEBERT LISE; KONG XIANQI (CA); NEUROCHEM INC (CA); CHALIFOUR ROBER) 7 June 2001 (2001-06-07) page 10; figures 1-4,6; examples I-III ---	1-22
X	WO 02 10354 A (CHRETIEN MICHEL; SEIDAH NABIL G (CA); CROMLISH JAMES A (CA); MONTR) 7 February 2002 (2002-02-07) * SEQ ID NO.3 * page 2; claims 1-17 ---	1-22
X	EP 0 683 234 A (TAKEDA CHEMICAL INDUSTRIES LTD) 22 November 1995 (1995-11-22) page 5 -page 9 ---	1-22
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

<sup>a</sup> Special categories of cited documents :

- \* A document defining the general state of the art which is not considered to be of particular relevance
- \* E earlier document but published on or after the international filing date
- \* L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
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- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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- \*Z\* document member of the same patent family

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 08320 A (MORPHOSYS PROTEINOPTIMIERUNG; KNAPPIK ACHIM (DE); PACK PETER (DE);) 6 March 1997 (1997-03-06) cited in the application abstract; table 2B	23-28
Y	page 194	1-22
X	--- O'NUALLAIN BRIAN ET AL: "Conformational Abs recognizing a generic amyloid fibril epitope" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 99, no. 3, 5 February 2002 (2002-02-05), pages 1485-1490, XP002211263 ISSN: 0027-8424 the whole document	1-22
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X	--- KNAPPIK A ET AL: "Fully synthesis human combinatorial antibody libraries (HuCAL) based on modular consensus frameworks and cds randomized with trinucleotides" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 296, no. 1, 2000, pages 57-86, XP000939143 ISSN: 0022-2836 cited in the application the whole document	23-28
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Y	WO 01 15655 A (MICHAELSON DANIEL M; UNIV RAMOT (IL)) 8 March 2001 (2001-03-08) page 8 -page 9; claims 1-4,23-26,66-68 page 22 page 24	1-22
Y	--- EP 1 125 905 A (PEPSCAN SYSTEMS B V) 22 August 2001 (2001-08-22) abstract column 1 -column 3; claims 1-18 ---	1-22
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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/01759

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 96 20218 A (EINSTEIN COLL MED; GHANBARI HOSSEIN A (US); DAVIES PETER (US); WOL) 4 July 1996 (1996-07-04) page 12; table A	1-22
A	SOLOMON B ET AL: "VACCINATION FOR THE PREVENTION AND TREATMENT OF ALZHEIMER'S DISEASE" DRUGS OF TODAY / MEDICAMENTOS DE ACTUALIDAD, J.R. PROUS SS.A. INTERNATIONAL PUBLISHERS, ES, vol. 36, no. 9, September 2000 (2000-09), pages 655-663, XP001030591 ISSN: 0025-7656 the whole document	1-22
P,X	WO 02 096937 A (HEBERT LISE; KONG XIANQI (CA); NEUROCHEM INC (CA); CHALIFOUR ROBER) 5 December 2002 (2002-12-05) * esp. SEQ ID NO:6 * page 57-58; claims 1,2; figure 1; examples I-V	1-22
P,X	WO 02 064734 A (SHARMA SHUBH D; SHI YI-QUN (US); PALATIN TECHNOLOGIES INC (US)) 22 August 2002 (2002-08-22) abstract; example 3; table 12	1-22
T	CRIBBS D H ET AL: "Adjuvant-dependent modulation of TH1 and TH2 responses to immunization with beta-amyloid" INTERNATIONAL IMMUNOLOGY, OXFORD UNIVERSITY PRESS, GB, vol. 15, no. 4, April 2003 (2003-04), pages 505-514, XP009013327 ISSN: 0953-8178 the whole document	1-22

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 03/01759

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-3 and claims 8, 9, 11-22 (all in part)  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-3 and claims 8, 9, 11-22 (all in part)

Present claims 1-3 and claims 8, 9, 11-22 as far as the refer to same subject-matter as claims 1-3 relate to an antibody which is defined by reference to the epitopes which are specifically recognized by said antibody.

However, the use of such parameters to define an antibody is considered to lead to a lack of clarity within the meaning of Article 6 PCT.

It is impossible to compare the parameters the applicant has chosen to define the subject-matter for which protection is sought with what is set out in the prior art. Any antibody cited in the prior art generated for binding to an epitope located between the amino acid positions 2 to 25 of the amyloid beta peptide (see e.g. either of the documents D1 to D3, D5 or D11 could bind to the amyloid beta fragments as defined in claims 1 to 3.

Moreover, the two region defined in said claims which form the epitope recognized by the antibodies are so close to each other that they do not necessarily form a discontinuous epitope.

Therefore, claims 1-3 and claims 8, 9, 11-22 are unclear and their subject-matter is not sufficiently disclosed as required by Art. 6 and 5 PCT.

Consequently, the search has been restricted to those claims wherein the antibodies are defined by technical features, namely their sequences.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/01759

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